compounds. The applicants however, avail themselves of the opportunity to traverse the Office's basis for the instant restriction on the grounds that a chemist would not find the instant invention to involve structurally distinct inventions. Compounds of Formula I are structurally related as well as related with respect to their pharmacological activity. Moreover, the instant restriction does not provide for the full scope of compounds claimed in the application.

Compounds of the instant invention are all substituted cyclopropane compounds and thus share a predominant structural feature, which common structural feature is at the core of each of the instant twelve (12) restriction groups. Moreover, these compounds possess the claimed α_4-ß$_2$ nicotinic receptor activity which activity is directly correlated with treatment of a well defined group of conditions, e.g., age-related cognitive disorders, Alzheimer's disease, dementia, Schizophrenia, attention-deficit/hyperactivity disorder, depression, Tourette's syndrome, anxiety, and neurodegeneration.

The applicants provided the Office with a Declaration, dated December 18, 2002, demonstrating this structure/function association. In the aforementioned Declaration, the applicants demonstrated that representative compounds in multiple instant restriction groups, possess significant α_4-ß$_2$ nicotinic receptor binding activity *in vitro*. What is more, representative compounds were shown to increase the *in vivo* release of acetylcholine in rat brains, thereby demonstrating dose-dependent α_4-ß$_2$ nicotinic receptor agonistic activity.

It is submitted that demonstrating common structural and pharmacological characteristics rebuts this new Office conclusion that the application represents multiple inventions. Absent contradictory evidence that those skilled in the art

would find the instant invention to consist of multiple inventions, it is submitted that the Office Requirement is not substantiated.

In an effort to assist the Office in formulating a more appropriate restriction group, and to advance the examination of the application, the applicants submit that instant Specification (Example 14), and Declaration of December 18, 2002, at the very least, demonstrate support for an expanded definition of "Y" in Restriction Group I as follows:

> *"claims 19-36, drawn to a compound of Claim 19 where p and n are as claimed, R_1 and R_2 are H, linear or branched (C_1-C_6)alkyl, aryl and aryl-(C_1-C_6)alkyl in which alkyl is linear or branched, X is equal to oxygen or sulphur, Y is equal to pyridyl* ***and C(O)A wherein A represents NR_3R_4 wherein R_3 and R_4 may be identical or different, each represent a linear or branched (C_1-C_6)alkyl, and pharmaceutical compositions."***

The slightly modified restriction group encompasses the compounds of Examples 11, 14, 18-20, 22-25, 28, 29, and 35; more than six of which compounds were demonstrated to possess significant α_4-$ß_2$ receptors nicotinic binding activity in the Declaration.

Alternatively, the applicants acknowledge that the previously elected species of Example 19 falls into Restriction Group I, therefore the applicants respond to the instant Restriction Requirement by electing Group I, *with traverse.* The applicants enquire as to the status of Group II of the Office Action dated June 18, 2002. The instant Restriction Groups do not cover the subject matter of original Restriction Group II.

In any event, Claims 19-29 and 31-36 in part, are rejected under 35 USC § 112, first paragraph, for lack of enablement. Specifically, the Office questions

the enablement of *"R_1 and R_2 forming together with nitrogen carrying them all 5 to 7 membered saturated carbocyclic systems, Y equal to all heteroaryl-(C_1-C_6)alkyl, R_3 and R_4 forming together with the nitrogen carrying them a monocyclic, or bicyclical (C_3-C_{10} system) and A equal to all heteroaryl rings."* The applicants submit that this phrase does not belong to elected Group I, but rather to non-elected Group II. Hence, reconsideration and withdrawal of the rejection is respectfully solicited.

Claim 31 in-part is rejected under 35 USC § 112, first paragraph, for indefiniteness because the Office considers it impossible to clearly define the scope of the claim to nicotinic ligands of α_4-ß$_2$ receptors. Similarly, Method Claim 32 is rejected for lack of enablement because the Office does not find the Specification to provide enablement for the numerous conditions claimed to be treatable.

The applicants previously submitted a Declaration (December 18, 2002) and literature review by a scientist skilled in the art which addressed the aforementioned rejections. Specifically, the Declarant provided empirical evidence that representative compounds commensurate with the scope of the elected invention, including the invention of the instant Restriction Group I, possess binding activity which one skilled in the art would find enabling of the claimed therapeutic activity. Representative compounds are shown in Table 1 of the Declaration to actively bind *in vitro* at central α_4-ß$_2$ nicotinic receptors in excised rat brains according to the assay presented at Example 42. Representative compounds are shown in Table 2 to increase the *in vivo* release of acetylcholine in rat brains under the protocol of Example 43, thereby demonstrating dose-dependent α_4-ß$_2$ nicotinic receptors agonist character. In the analgesic model of Example 44, representative compounds of the instant

invention are shown to antagonize phenyl-p-benzoquinone (PBQ) induced abdominal contractions in mice in a dose-dependent manner, demonstrating *in vivo* antalgic activity. Finally, the Declarant presented *in vivo* social recognition data in rats for representative compounds of the instant invention in Table 4. Representative compounds are shown in a dose-dependent manner to significantly enhance social memorization under the protocol of Example 45. Thus, it is submitted that the applicants have supplied enabling disclosure of the claimed α_4-ß$_2$ nicotinic receptor activity, which activity is directly correlated with therapeutic efficacy.

Alternatively, if it is still the position of the Office that the 35 USC § 112, first paragraph rejections are maintained, irrespective of the election and the demonstration of the Declaration, the applicants respectfully request that the Examiner provide the basis upon which the applicant's Declaration was found to be inadequate to overcome these rejections. In the absence of such basis, the applicants hereby solicit reconsideration and withdrawal of the enablement and indefiniteness rejections.

Finally, Claims 35 and 36 are rejected under 35 USC § 112, second paragraph for failing to claim with particularity because US patent Office procedure does not accept *"useful for"* language in pharmaceutical composition claims. The applicants submit that the *Response and Amendment of December 18, 2002*, requested cancellation of Claims 35 and 36, thereby obviating the rejection.

* * * * *

Accordingly, entry of the present amendment, reconsideration of all grounds of objection and rejection, withdrawal thereof, and passage of this application to issue are all hereby respectfully solicited.

It should be apparent that the undersigned attorney has made an earnest effort to place this application into condition for immediate allowance. If he can be of assistance to the Examiner in the elimination of any possibly-outstanding insignificant impediment to an immediate allowance, the Examiner is respectfully invited to call him at his below-listed number for such purpose.

Allowance is solicited.

Respectfully submitted,
THE FIRM OF HUESCHEN AND SAGE

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THE COMMISSIONER IS HEREBY AUTHORIZED TO CHARGE ANY FURTHER OR ADDITIONAL FEES WHICH MAY BE REQUIRED (DUE TO OMISSION, DEFICIENCY, OR OTHERWISE), OR TO CREDIT ANY OVERPAYMENT, TO DEPOSIT ACCOUNT NO. 08,3220.